

We claim:

1. An isolated nucleic acid encoding a polypeptide comprising an alpha subunit forming a eag-like potassium channel having the characteristic of slowly activated outward rectification selected from the group consisting of *elk1*, *elk2* and *eag2*.
5
2. The isolated nucleic acid according to claim 1 encoding a polypeptide forming a potassium channel for which the activation time constant for outward rectification is
- 10 3. The isolated nucleic acid according to claim 2 wherein the activation time constant for outward rectification is at least 100 ms at 0 mV with a threshold activation at -40 mV.
4. The isolated nucleic acid according to claim 2 wherein
15 the activation time constant for outward rectification is 676 ± 37 ms at 0 mV with a threshold activation at -40 mV at about pH 7.
5. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a polypeptide having a molecular weight of
20 between 100 to 150 kDa.
6. The isolated nucleic acid of claim 1, wherein the polypeptide has a molecular weight of about 123 kDa.
7. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human *elk1*.
- 25 8. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes rat *elk1*.
9. The isolated nucleic acid of claim 1, wherein the nucleic acid encodes human *elk2*.
10. The isolated nucleic acid of claim 1, wherein the nucleic
30 acid encodes human *eag2*.
11. The isolated nucleic acid sequence of claim 7, wherein the nucleic acid has a nucleotide sequence of SEQ ID No:1.

12. The isolated nucleic acid sequence of claim 8 wherein the nucleic acid is at least 80% homologous to SEQ ID NO:1.
13. The isolated nucleic acid of claim 7, wherein the nucleic acid is isolated from superior cervical ganglia, coeliac ganglia, superior mesenteric ganglia, foetal brain, adrenal or stellate ganglia by PCR using primers that selectively hybridize under stringent hybridization conditions to a pair of primers:
- 5' TTY AAR RCN RYN TGG GAY TGG 3' (SEQ ID No:5) and
3' RTA CCA DAT RCA NGC NAG CCA RTG 5' (SEQ ID No:6)
and amplified using a pair of primers:
- 5' CGG GAT CCT TGT GGA CAA AC 3' (SEQ ID NO:7)
3' TTC AGG AAT GAC AAC CAG GC 5' (SEQ ID NO:8)...
14. The isolated nucleic acid of claim 8 encoding a polypeptide and specifically hybridizes under stringent conditions to SEQ ID No:1.
15. The isolated nucleic acid of claim 8, wherein said nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleotide sequence of SEQ ID No:1.
16. The isolated nucleic acid of claim 1, wherein said nucleic acid encodes the polypeptide SEQ ID NO:3.
17. The isolated nucleic acid of claim 1, wherein said nucleic acid comprises the partial sequence SEQ ID NO:13.
18. The isolated nucleic acid of claim 15, wherein the nucleic acid is isolated from superior cervical ganglia by PCR using primers that selectively hybridize under stringent hybridization conditions to a pair of primers:
- 5' TTY AAR RCN RYN TGG GAY TGG 3' (SEQ ID No:5) and
3' RTA CCA DAT RCA NGC NAG CCA RTG 5' (SEQ ID No:6)
and amplified with a pair of primers:

5' GTG ATA CCC ATA AAG AAT GAG 3' (SEQ ID NO:9)

3' CGG AAA TTC AGC ACA ATG TC 5' (SEQ ID NO:10).

19. The isolated nucleic acid of claim 1, wherein said
nucleic acid partially encodes the polypeptide SEQ ID
NO:4.

20. The isolated nucleic acid of claim 1, wherein said
nucleic acid comprises the partial sequence SEQ ID NO:14.

21. The isolated nucleic acid of claim 18, wherein the
nucleic acid is isolated from brain tissue by PCR using
primers that selectively hybridize under stringent
hybridization conditions to a pair of primers:

5' TTY AAR RCN RYN TGG GAY TGG 3' (SEQ ID No:5) and

3' RTA CCA DAT RCA NGC NAG CCA RTG 5' (SEQ ID No:6)

and amplified by PCR using a pair of primers:

5' CGG GAT CCT TGT GGA CAA AC 3' (SEQ ID NO:7)

3' TTC AGG AAT GAC AAC CAG GC 5' (SEQ ID NO:8).

22. An isolated polypeptide forming a eag-like potassium
channel having the characteristic of slowly activated
outward rectification selected from the group consisting
of *elk1*, *elk2* and *eag2*.

23. The isolated polypeptide according to claim 21 forming a
eag-like potassium channel for which the activation time
constant for outward rectification is

24. The isolated polypeptide according to claim 21 wherein
the potassium channel has an activation time constant for
outward rectification of 676 ± 37 ms at 0 mV with a
threshold activation at -40 mV at about pH 7.

25. The isolated polypeptide of claim 21, wherein the
polypeptide is rat *elk1*.

26. The isolated polypeptide of claim 21, wherein the
polypeptide is human *elk1*.

27. The isolated polypeptide of claim 21, wherein the polypeptide is human elk2.
28. The isolated polypeptide of claim 21, wherein the polypeptide is human eag2.
- 5 29. The isolated polypeptide of claim 21 wherein the amino acid sequence of the polypeptide is SEQ ID NO:2.
30. The isolated polypeptide of claim 21 wherein the partial amino acid sequence of the polypeptide is SEQ ID NO:3.
31. The isolated polypeptide of claim 21 wherein the partial
10 amino acid sequence of the polypeptide is SEQ ID NO:4.
32. An expression vector comprising the nucleic acid of claim 1.
33. An expression vector comprising the nucleic acid of claim 4.
- 15 34. An expression vector comprising the nucleic acid of claim 5.
35. An expression vector comprising the nucleic acid of claim 6.
36. An expression vector comprising the nucleic acid of claim
20 7.
37. An expression vector comprising the nucleic acid of claim 16.
38. An expression vector comprising the nucleic acid of claim 19.
- 25 39. A host cell transfected with the vector of claim 31.
40. A host cell transfected with the vector of claim 32.
41. A host cell transfected with the vector of claim 33.
42. A host cell transfected with the vector of claim 34.
43. A host cell transfected with the vector of claim 35.
- 30 44. A host cell transfected with the vector of claim 36.
45. A host cell transfected with the vector of claim 37.

46. A method for identifying a compound that modulates ion flux through a slowly activated outward rectifier potassium channel selected from the group consisting of elk1, elk2, eag2, the method comprising the steps of:
- 5 (i) contacting the compound with a eukaryotic host cell or cell membrane in which has been expressed a polypeptide forming a potassium channel having the characteristic of slowly activated outward rectification; and
- 10 (ii) determining the functional effect of the compound upon the cell or cell membrane expressing the potassium channel.
47. The method of claim 38, wherein the eukaryotic host cell is *Xenopus* oocyte.
- 15 48. The method of claim 38, wherein the functional effect is determined by measuring changes in current or voltage.
49. The method of claim 38, wherein the potassium channel polypeptide is recombinant.
50. The method of claim 38, wherein the potassium channel is
- 20 heteromeric.
51. The method of claim 38, wherein the potassium channel polypeptide is human elk1.
52. The method of claim 38, wherein the potassium channel polypeptide has an amino acid sequence of SEQ ID No:2.
- 25 53. A method of detecting the presence of elk1 in mamalian tissue selected from the group consisting of superior cervical ganglia, coeliac ganglia, superior mesenteric ganglia, foetal brain, adrenal and stellate ganglia, the method comprising the steps of
- 30 (i) isolating a biological sample from the mammalian tissue,
- (ii) contacting the biological sample with a elk1

specific reagent that selectively associates with elk1;
and

(iii) detecting the level of elk1 specific reagent that
selectively associates with the sample.

5 54. The method of claim 52, wherein the elk1-specific reagent
is selected from the group consisting of: elk1, specific
oligonucleotide primers, and elk1 nucleic acid probes.

55. In a computer system, a method of screening for mutations
of human *eag*-like genes selected from the group
10 consisting of *elk1*, *elk2* and *eag2*, the method comprising
the steps of:

(i) entering into the computer system a first nucleic
acid sequence encoding a slowly activated outward
rectifier potassium channel polypeptide, said first
15 nucleic acid sequence having a nucleotide sequence
selected from the group consisting of of SEQ ID No:1,
comprising partial SEQ ID NO:13, and partial SEQ ID NO:
14 and conservatively modified versions thereof;
(ii) comparing the first nucleic acid sequence with a
20 second nucleic acid sequence having substantial identity
to the first nucleic acid sequence; and
(iii) identifying nucleotide differences between the
first and second nucleic acid sequences.

56. The method of claim 54, wherein the second nucleic acid
25 sequence is associated with a disease state.

57. A computer readable substrate comprising the first amino
acid sequence of claim 24.

58. A computer readable substrate comprising the first amino
acid sequence of claim 25.

30 59. A computer readable substrate comprising the first amino
acid sequence of claim 26.

60. A computer readable substrate comprising the first amino acid sequence of claim 27.

61. In a computer system, a method for identifying a three-dimensional structure of EAG-like polypeptides selected from the group consisting of elk1, elk2, eag2, the method comprising the steps of:

(i) entering into the computer system an amino acid sequence of at least 10 amino acids of a potassium channel peptide or at least 30 nucleotides of a gene encoding the polypeptide, the polypeptide having a partial amino acid sequence selected from a group consisting of a part of SEQ ID No: 2, SEQ ID NO:3, SEQ ID NO:4 and conservatively modified versions thereof; and

(ii) generating a three-dimensional structure of the polypeptide encoded by the amino-acid sequence.

62. The method of claim 60, wherein said amino acid sequence is a primary structure and wherein said generating step includes the steps of:

(i) forming a secondary structure from said primary structure using energy terms determined by the primary structure; and

(ii) forming a tertiary structure from said secondary structure using energy terms determined by said secondary structure.

63. The method of claim 61, wherein said generating step further includes the step of forming a quaternary structure from said tertiary structure using anisotropic terms encoded by the tertiary structure.

64. The method of claim 60, further comprising the step of identifying; regions of the three-dimensional structure of the protein that bind to ligands and using the regions to identify ligands that bind to the polypeptide.

65. A computer readable substrate comprising the three dimensional structure of the polypeptide of claim 24.
66. A computer readable substrate comprising the three dimensional structure of the polypeptide of claim 25.
- 5 67. A computer readable substrate comprising the three dimensional structure of the polypeptide of claim 26.
68. A computer readable substrate comprising the three dimensional structure of the polypeptide of claim 27.